

Invited Commentary

Molecular Genetics of Meningiomas

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The molecular changes for tumorigenesis in meningiomas are only half known. In general, there are three approaches to investigations: analysing the genetic changes required for tumorigenesis, studying syndromes of familial brain tumours that may include meningiomas, and investigating specific genetic defects that may correlate with tumour grade and clinical behaviour.

For the first aim, a wide variety of techniques, from conventional molecular techniques to newer techniques such as comparative genomic hybridization and expression microarray, have been used. The only confirmed tumour-associated gene in meningioma is the neurofibromatosis 2 gene (*NF2*) located on chromosome 22q12. About 60% of sporadic meningiomas exhibit either mutations in *NF2* or deletions in 22q or even monosomy and, in many instances, nicely follow the two-hit model of tumour suppressor gene inactivation.¹ A meningioma-prone *NF2* knockout mouse was recently developed and will serve as a useful model for testing novel therapies.² Allelic loss has also been documented in 1p, 10q, 14q, 6q, 9q, 17q and 18q. These regions may harbour potential tumour suppressor sites that need to be delineated. Recent studies are highly suggestive that another protein 4.1 family member (the *NF2* product, merlin being one), 4.1R encoded by a gene at 1p36, is a tumour suppressor.³ So far, no known oncogene has been identified for meningiomas. In spite of the small proportion of cases with 17p loss, studies of the *p53* gene have not shown significant gene alterations, a finding similar to that of Das et al in this issue of the *Asian Journal of Surgery*. It has been clear to most investigators in this field that the *p53* gene is not a major gene of interest; few benign tumours elsewhere possess *p53* mutations. Meningiomas occur in both type 1 (*NF1*) and type 2 neurofibromatosis for which germline mutations play a major role in tumorigenesis. As *NF1* is a very large gene, it has, so far, not been studied in sporadic meningiomas, although aberrant splicing has been suggested as a mechanism of

reduced expression.⁴

A number of cytogenetic or molecular abnormalities are associated with meningioma progression or high-grade histology. In most instances, the relevant candidate genes remain a mystery. For example, 14q deletions are common in high-grade meningiomas or meningiomas that subsequently recur⁵ and the loss of the *p16* gene on 9p21 is associated with anaplastic meningiomas and poor survival.⁶⁻⁹ The powerful technique of expression profiling used to examine thousands of genes simultaneously has also been used with meningiomas, but it remains to be seen whether it will yield useful data towards patient prognosis or management.¹⁰

References

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